Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte RACHEL MEYERS

Appeal No. 2003-1820
Application No. 09/464,039

ON BRIEF

Before WILLIAM F. SMITH, ADAMS, and GRIMES Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 63-67, 77-79 and 87-104, which are all the claims pending in the application.

Claims 63, 77, 79, 87 and 88 are illustrative of the subject matter on appeal and are reproduced below:

87. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
a) the nucleotide sequence set forth in SEQ ID NO:8;
b) the nucleotide sequence of the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-2170;
c) a nucleotide sequence encoding the amino acid sequence set forth in SEQ ID NO:7;
d) a nucleotide sequence encoding the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-2170; and

e) a nucleotide sequence complementary to a nucleotide sequence of a), b), c), or d).

63. The nucleic acid molecule of claim 87 further comprising vector nucleic acid sequences.

77. A method for detecting the presence of a nucleic acid molecule of claim 87 in a sample, said method comprising the steps of contacting the sample with a nucleic acid probe which selectively hybridizes to the nucleic acid molecule and determining whether the nucleic acid probe binds to the nucleic acid molecule in the sample; wherein said nucleic acid probe is selected from the group consisting of:
a) the nucleotide sequence set forth in SEQ ID NO:8;
b) the nucleotide sequence of a fragment of the nucleotide sequence set for[th] in SEQ ID NO:8, wherein said fragment comprises at least 417 contiguous nucleotides of the nucleotide sequence set forth in SEQ ID NO:8;
c) a nucleotide sequence having at least 70% sequence identity to the nucleotide sequence set forth in SEQ ID NO:8; and
d) a nucleotide sequence complementary to a nucleotide sequence of a), b), or c).

79. A kit for use in the method of claim 77, wherein said kit comprises at least one nucleic acid probe of claim 77 and instructions for use in the method of claim 77.

88. An isolated nucleic acid molecule having a nucleotide selected from the group consisting of:

a) a nucleotide sequence encoding a polypeptide having dehydrogenase activity, wherein said nucleotide sequence has at least 70% sequence identity with the nucleotide sequence set forth in SEQ ID NO:8; and
b) a nucleotide sequence complementary to the nucleotide sequence of a).

The references relied upon by the examiner are[1]:

Duester, "Families of retinoid dehydrogenases regulating vitamin A function: Production of visual pigment and retinoic acid," Eur. J. Biochem., Vol. 267, pp. 4315-24 (2000)

Rosenberg et al. (Rosenberg), "Gene Therapist, Heal Thyself," Science, Vol. 287, p 1751 (2000)

Wood, "Phenotype Assessment: Are You Missing Something?," Comp. Med., Vol. 50, No. 1, pp. 12-15 (2000)

GROUNDS OF REJECTION

Claims 63-67, 77-79 and 87-104 stand rejected under 35 U.S.C. § 101 as the claimed invention lacks patentable utility.

Claims 63-67, 77-79 and 87-104 stand rejected under 35 U.S.C. § 112, first paragraph as based on a specification that fails to enable how to make and use the claimed invention.

Claims 88-92 stand rejected under 35 U.S.C. § 112, first paragraph as based on a specification that fails to provide an adequate written description of the claimed invention.

Claim 79 stands rejected under 35 U.S.C. § 112, second paragraph as indefinite in the recitation of the phrase "instructions for use."

We reverse.

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[1] While the examiner states (Answer, page 3), "[n]o prior art is relied upon by the examiner in the rejection of the claims under appeal," the examiner relied upon the references listed herein in the Answer and during prosecution. See e.g., Paper No. 9, pages 3 and 6; and Paper No. 13, pages 3 and 7. Accordingly, it appears that the examiner's statement is in error.

DISCUSSION

Claim Definiteness:

While the examiner recognizes that the limitations of claim 79 relate the claimed kit to the method of claim 77, the examiner asserts (Answer, page 13), "[c]laim 79 is indefinite because it is unclear what are [sic] the 'instructions for use' in this context." In clarifying this assertion, the examiner states (id.), "the scope of [the] instructions for use is not limited to the subject matter of claim 77[,] [f]or example, instructions can include additional products and methods that are not described in the instant specification."

As we understand the examiner's statements, it is the examiner's opinion that even though the kit can be used in the method of claim 77, since the instructions for the use of the kit may make reference to non-disclosed reagents or recite additional method steps, the kit set forth in claim 79 is indefinite. We disagree. As appellant explains (Brief, page 27), claim 79 is drawn to a

> "kit for use in the method of claim 77, wherein said kit comprises at least one nucleic acid probe of claim 77 and instructions for use in the method of claim 77." ... [C]laim 77 specifically recites the essential steps of the claim[ed] method of detection, and one of skill in the art would recognize what is intended by the phrase "instructions for use in the method of claim 77."

The mere possibility that the instructions included with a kit may include additional method steps or refer to other ingredients other than those set forth in the claimed invention does not necessarily make the description indefinite or extend it beyond appellant's intent. As set forth in Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030 (Fed. Cir. 1991):

> The statute requires that "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." A decision as to whether a claim is invalid under this provision requires a determination whether those skilled in the art would understand what is claimed.

In our opinion, a person of ordinary skill in the art would understand what is claimed. Accordingly, we reverse the rejection of claim 79 under 35 U.S.C. § 112, second paragraph.

Utility:

The PTO has the initial burden of challenging a patent applicant's presumptively correct assertion of utility. In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995). If the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility, however, the burden shifts to the applicant to submit evidence sufficient to convince such a person of the invention's asserted utility. Id.

On this record, appellant discloses (specification, page 1), "[t]he present invention relates to newly identified human alcohol dehydrogenases (ADHs) belonging to the superfamily of mammalian dehydrogenases/reductases." In this regard, appellant discloses (specification, page 10, emphasis removed), "Figure 15 shows the nucleotide sequence (SEQ ID NO:7) and the deduced amino acid sequence (SEQ ID NO:8) of the novel 21612 ADH."

According to appellant (Brief, bridging paragraph, pages 3-4), "[t]he function of the novel 21612 polypeptide was determined by comparing the 21612

amino acid sequence set forth in SEQ ID NO:7 to the Pfam database of protein families." As appellant explains (Brief, page 4),

> Pfam alignments do not display homology between pairs of sequences but rather display the fit of a particular query sequence to a particular protein family model. Thus the measure of the strength of a match between the query sequence and the Pfam consensus alignment is the Pfam bit score, which shows the statistical significance of the fit between the query sequence and the Pfam consensus alignment.

According to appellant (Brief, page 5), the Pfam bit score for the 21612 polypeptide is 145, which as appellant explains (id.), "means that the 21612 amino acid sequence is 2^{145} (4.46×10^{43}) times more likely to belong to the short chain dehydrogenase family than to contain the amino acid sequence ... by chance."[2]

However, notwithstanding appellant's arguments and Pfam data, the examiner asserts (id.), "[t]he recited SEQ ID NO(s) are simply computer-generated hypotheses wherein no biological function[3] has been established." The examiner, however, offers no evidence to suggest that appellant's Pfam analysis is not an art-accepted method of determining protein function. Instead, the examiner asserts (id., emphasis removed), "[t]he specification fails to show a single working example that establishes that ... SEQ ID NO: 8 which encodes the amino acid sequence of SEQ ID NO:7 is a member of [the] [a]lcohol dehydrogenase ... family, such as by any substantial sequence homology and/or

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[2] We recognize appellant's reference (Brief, page 5), to "the Pfam documentation available at http://pfam.wustl.edu/faq.shtml...."

[3] With reference to Duester, the examiner finds (Answer, page 4), "[i]t is known in the art that [a]lcohol dehydrogenase (ADH) constitutes a complex enzyme system with different forms and extensive multiplicity and the range of ... biochemical reactions which can be catalyzed by ADH is extremely wide."

functional assay of the protein." In our opinion this assertion, in no way detracts from the weight of appellant's evidence relating to the Pfam bit score for the 21612 polypeptide, placing appellant's polypeptide in the ADH family of proteins, which according to appellant (Brief, page 11), and undisputed by the examiner, is a class of polypeptides having well-established utility.

We also note the examiner's reference (Answer, page 4), to two results (ACC. No. T19954 and ACC. No. AA622988) from an "Office sequence search" to support his assertion that "it is unclear that any ADH-like activity could be attributed to the deduced amino acid sequence of the claimed nucleic acid sequence." However, when confronted with appellant's explanation (see Brief, pages 5-6) of how these two search results support appellant's asserted utility, the examiner switches horses and directs our attention (Answer, pages 8 and 9) to a "US-PTO Pfem [sic]-analysis" which the examiner presents for the first time in the Answer. Not only is the examiner's reliance on this Pfam analysis not properly before this panel[4], for the following reasons we find it inadequate to support the examiner's assertion.

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[4] See MPEP 1208.01:

> A new prior art reference cited for the first time in an examiner's answer generally will constitute a new ground of rejection. If the citation of a new prior art reference is necessary to support a rejection, it must be included in the statement of rejection, which would be considered to introduce a new ground of rejection. Even if the prior art reference is cited to support the rejection in a minor capacity, it should be positively included in the statement of rejection. In re Hoch, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n. 3 (CCPA 1970).

Cf. 37 CFR 1.193(2) (An examiner's answer must not include a new ground of rejection....").

With reference to the Pfam analysis illustrated on page 9 of the Answer, the examiner asserts (Answer, page 8),

> [e]ven though the applicant asserts that the amino acid sequences [sic] of SEQ ID NO:7 contain a[n] ADH short chain dehydrogenase-like motif ..., the applicant fails to consider that besides the presence of an ADH shortchain dehydrogenase-like motif the amino acid sequence of SEQ ID N[O]:7 also contain[s] a SCP2 domain ... that is involved in the binding of [s]terols."

From this the examiner reasons (id.), "[c]onsidering the presence of two functionally distinct domains the applicant fails to provide any evidence that the amino acid sequences [sic] of SEQ ID NO:7 has any alcohol dehydrogenase-like activity based upon any alcohol dehydrogenase specific substrate specificity." The examiner, however, fails to explain why a Pfam bit score of 76.5 (see Pfam illustration, Answer, page 9) for the SCP domain would outweigh the Pfam bit score of 102[5] (see id.) for the ADH domain. As discussed, supra, appellant explains (Brief, page 5), that the higher the Pfam bit score, the more likely the polypeptide will belong to a particular protein family than to contain the amino acid sequence by chance. Thus, according to the examiner's Pfam analysis (Answer, page 9), appellant's polypeptide sequence is 2^{102} (5.07×10^{30}) times more likely to belong to the short chain dehydrogenase family than to contain the amino acid sequence by chance, while it is $2^{76.5}$ (1.07×10^{23}) times more likely to belong to the SCP2 family than to contain the amino acid sequence by chance. The examiner fails to offer any explanation as to why his Pfam analysis would lead a person of ordinary skill in the art to believe that appellant's polypeptide is

[5] Or according to appellant's Pfam analysis a bit score 145.

more likely to be a member of the SCP2 family, than a member of the ADH family.

Further, even if appellant's polypeptide contained both an ADH domain and a SCP2 domain, the examiner fails to provide any factual evidence to establish that appellant's polypeptide would not have utility as an ADH. According to appellant's specification (page 2), most dehydrogenase proteins possess at least two domains: the first domain comprising the coenzyme binding site, and the second domain comprising the substrate binding site. This latter domain determines the substrate specificity and contains the amino acids involved in catalysis. Both the examiner's (Answer, page 9), and appellant's (Brief, appendix A), Pfam analysis illustrate that the ADH domain of the claimed polypeptide is at the amino-terminal end of the polypeptide. According to the examiner's Pfam analysis (Answer, page 9), the SCP2 domain is present in the carboxy-terminal end of the polypeptide. This appears to be consistent with appellant's disclosure that most dehydrogenase proteins possess at least two domains. Accordingly, we are not persuaded by the examiner's arguments with regard to the Pfam analysis.

We are also not persuaded by the examiner's statement (Answer, page 8), that appellant's "arguments would be persuasive if they have demonstrated the catalytic oxidation of a single SDR [short chain dehydrogenase] substrate using the claimed amino acid sequences." The examiner, however, fails to identify any rule of law, and we know of none, that requires appellant's specification to contain a working example. Cf. In re Strahilevitz, 668 F.2d 1229,

1232, 212 USPQ 561, 563 (CCPA 1982) ("examples are not required to satisfy section 112, first paragraph.").

In addition, we are not persuaded by the examiner's suggestion (id., emphasis added) that since appellant's polypeptide is 418 residues long and SDRs "typically have subunits containing approximately 250[6] residues," appellant's polypeptide is not an ADH. The examiner, however, fails to establish a nexus between a subunit (e.g. a domain) of a polypeptide and the full-length polypeptide. Stated differently, the examiner fails to provide any evidence demonstrating that proteins in the SDR family are typically only about 250 residues in length.

For the foregoing reasons, it is our opinion that the examiner failed to provide the evidence necessary to meet his burden of challenging applicant's presumptively correct assertion of utility. Accordingly, we reverse the rejection of claims 63-67, 77-79 and 87-104 under 35 U.S.C. § 101.

Enablement:

To the extent that the examiner's assertions are simply a corollary to his finding of a lack of utility (See e.g., Answer, page 10) our conclusion with regard to the rejection under 35 U.S.C. § 101; also applies to the rejection under 35 U.S.C. § 112. We note, however, that the examiner has made additional arguments with regard to the enablement rejection. Accordingly, we focus our attention on these additional arguments. We note, however, "[w]hen rejecting a claim under the enablement requirement of section 112, the PTO bears an initial

burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification." In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Carrying that burden requires evidence or sound scientific reasoning showing that practicing the full scope of the claims would have required undue experimentation. See In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) ("[E]nablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.' . . . That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'").

On this record, the examiner finds (Answer, page 5, emphasis added), "the claimed invention is drawn to the polypeptide encoded by the nucleic acid sequences which hybridize to nucleic acid sequence of SEQ ID N[O]:8 or have 70-90% sequence identity to SEQ ID NO:8 (see claims 88-90)[.]" In this regard, the examiner finds (id.), "[t]he variants as claimed encompass 10-30% nucleotide sequence variation over the entire length of SEQ ID NO:8." Thus, the examiner concludes (id.), "[t]he claimed invention is not enabled in view of [sic] lack of teachings in the specification as filed regarding what additional sequences may be added, deleted or substituted to those specifically disclosed, such that asserted [sic] utility discussed in the section 101 rejection above would be recognized as specific and/or substantial."

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[6] The examiner relies on page 4316 of Duester to support this assertion.

At the outset we recognize the examiner's focus on claims 88-90. Claims 77-79, and 98-100, however, also contain similar "% identity" language, and claim 91 is drawn to a nucleic acid molecule that hybridizes to the nucleotide sequence set forth in SEQ ID NO:8. The examiner, however, makes no reference to claims 77-79, 91 or 98-100.[7] Accordingly, it appears that the examiner has treated the claims in this application in an inconsistent manner. Further, each of claims 88-90 requires that the nucleotide sequence encode a polypeptide having dehydrogenase activity. Thus, despite some degree of variation in the nucleotide sequence the claimed nucleic acid molecule must encode a polypeptide having dehydrogenase activity.

We are also not persuaded by the examiner's statement (Answer, page 5), "[i]t is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if...." The examiner's reference to "general knowledge," does not fulfill his obligation to cite references to support his conclusions. Cf. In re Lee, 277 F.3d 1338, 1344, 61 USPQ2d 1430, 1434 (Fed. Cir. 2002). In our opinion, the examiner failed to meet his burden of providing the evidence necessary to establish a lack of an enabling description.

In addition, we find it unclear, as to why the examiner believes that to enable the claimed invention the specification must disclose the role, if any, that the claimed polypeptides play in a disease. Answer, page 6. As set forth above,

[7] Cf. the examiner's rejection of claims 88-92 under the written description provision of 35 U.S.C. 112, first paragraph, infra, where the examiner focuses our attention on the "% sequence identity."

appellants have asserted that alcohol dehydrogenases, as a class, have a well-established utility. Brief, page 11. The examiner has not disputed this assertion.

Nevertheless, it may be that the examiner linked this argument to his belief that since claims 65-67 and 95-97 are drawn, inter alia, to a host cell containing nucleic acid these claims read on gene therapy, and/or the production of transgenic animals. See e.g., Answer, page 6. However, no claim on appeal is directed to the treatment or diagnosis of a disease, nor is any claim on appeal directed to a gene therapy method, or method of producing a transgenic animal. See Brief, page 20, wherein appellant asserts "the claims are not directed to methods of gene therapy or to methods of producing a transgenic animal having a particular phenotype but instead are directed to host cells containing specified nucleic acid molecules."

While it is true that appellant's specification discloses the use of ADH polynucleotides for use in "gene therapy" (see e.g., specification, page 79 and 88), and in the production of transgenic animals (see e.g., specification, page 68), we remind the examiner that "[t]he enablement requirement is met if the description enables any mode of making and using the invention." Johns Hopkins Univ. v. CellPro Inc., 152 F.3d 1342, 1361, 47 USPQ2d 1705, 1714 (Fed. Cir. 1998) (quoting Engel Indus., Inc. v. Lockformer Co., 946 F.2d 1528, 1533, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991)).

According to appellant's specification (page 88), host cells are useful for: "producing ADH proteins or polypeptides"; "conducting cell-based assays involving the ADH or ADH fragments"; "identifying ADH mutants"; and etc. The examiner has not explained why the specification does not enable these uses of the host cells. Absent evidence to the contrary from the examiner, we have no reason to doubt appellant's presumptively enabled specification. In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). Since the specification describes one method of making and using the invention of claims 65-67 and 95-97, it enables those claims, whether or not the claimed method is also enabled for use in gene therapy, or in the production of transgenic animals.

For the foregoing reasons we reverse the rejection of claims 63-67, 77-79 and 87-104 under the enablement provision of 35 U.S.C. § 112, first paragraph.

Written Description:

The examiner has the initial burden of establishing that appellant's specification does not satisfy the written description provision of 35 U.S.C. 112, first paragraph. In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976).

According to the examiner (Answer, page 6), claims 88-92 "are drawn to a nucleotide sequence encoding a polypeptide having dehydrogenase activity, wherein the nucleotide has at least 70-90% sequence identity with [the]

nucleotide sequence of SEQ ID NO:8." In this regard, the examiner finds (id.), "[t]he specification as [filed] fails to disclose any and all variant [sic] of human alcohol dehydrogenase comprising the nucleic acid sequence of SEQ [ID NO:] 8, which encodes the amino acid sequences [sic] of SEQ ID NO:7."

While the examiner recognizes (Answer, page 12, emphasis removed), "possession may be shown ... by describing the invention with sufficient relevant identifying characteristics ... such that a person skilled in the art would recognize that the inventor had possession of the claimed invention," the examiner asserts (Answer, bridging sentence, pages 12-13), "the 21612-polynucleotides has [sic] been defined only by a statement of function of short chain alcohol dehydrogenase activity, which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics." According to the examiner (Answer, page 7), appellant discloses SEQ ID NO:8, and "proposes to discover other members of the genus using hybridization procedure [sic]."

Initially, we agree with appellant (Brief, page 21),

> "the [e]xaminer has presented no evidence to demonstrate that one of skill [in] the art would doubt the credibility of [a]pplicant's assertion that the 21612 polypeptide functions as a dehydrogenase. Accordingly, the premise on which the rejection is based, i.e. that the 21612 polypeptide does not have dehydrogenase activity, is not supported by the evidence of record." Brief, page 21.

In addition, appellant argues (Brief, page 22), claims 88-92 "recite the identifying structural characteristics that define each genus of nucleotide sequences" Specifically, appellant points out (Brief, bridging paragraph, pages 22-23),

> [c]laims 88-90 recite nucleotide sequences having at least 70%, 80%, or 90% sequence identity with the nucleotide sequence set forth in SEQ ID NO:8, claim 91 recites nucleotide sequences that hybridize to the nucleotide sequence set forth in SEQ ID NO:8 under specified conditions, and claim 92 recites nucleotide sequences encoding a fragment of the amino acid sequence set forth in SEQ ID NO:7 or the amino acids [sic] sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-2170....

In addition, appellant points out (Brief, page 23), "claims 88-92 recite that the variants and fragments have dehydrogenase activity."

On this record, we have the amino acid sequence of the protein, SEQ ID NO:7. In In re Wallach, No. 03-1327, 2004 WL 1780989, at *3 (Fed. Cir., Aug. 11, 2004), our appellate reviewing court found

> the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art ... [in 1995] may have therefore been in possession of the entire genus of DNA sequences that can encode the ... protein sequence, even if individual species within that genus might not have been described or rendered obvious.

In this regard, we note that the instant application was filed in 1999. Thus, it appears that appellant was in possession of all variants within the genus of DNA sequences that can encode the protein sequence set forth in SEQ ID NO:7.

Further, as appellant points out (Brief, page 15), the claims are limited to nucleotide sequences meeting both the structural requirements of these claims and the claimed functional requirement – having dehydrogenase activity. Both appellant's and the examiner's Pfam analysis (see Answer, page 9) demonstrate that a person of ordinary skill in the art at the time the invention was made would recognize the relevant structural characteristics of appellants' claimed invention that are necessary to place a polypeptide encoded by a nucleic acid variant of SEQ ID NO:8 in the dehydrogenase family of proteins. The examiner provides no evidence on this record that the Pfam analysis cannot be used to assign a function to a protein.

Further, as discussed supra, while the examiner focuses our attention on claims 88-92, we note that claims 77-79, and 98-100 also contain similar "% identity" language. The examiner, however, makes no reference to claims 77-79 or 98-100. Accordingly, it appears that the examiner has treated the claims in this application in an inconsistent manner.

For the foregoing reasons, it is our opinion that the examiner failed to meet his burden of providing the evidence necessary to maintain the rejection of claims 88-92 under the written description provision of 35 U.S.C. § 112, first paragraph. Accordingly, we reverse the written description rejection.

SUMMARY

For the foregoing reasons, it is our opinion that the examiner failed to meet his evidentiary burden in each of the rejections of record. Accordingly, all rejections of record are reversed.

REVERSED

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

BOARD OF PATENT APPEALS AND INTERFERENCES

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Paper No. 27

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte YUEJIN SUN, BRIAN R. DILKES, BRIAN A. LARKINS, KEITH S. LOWE, WILLIAM J. GORDON-KAMM and RICARDO A. DANTE

Appeal No. 2003-1993
Application No. 09/470,526

ON BRIEF

Before WILLIAM F. SMITH, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 2-11, 31, 33 and 35-36 which are the claims on appeal in this application. Claims 14, 32 and 37 have been allowed.

Claim 31 is illustrative of the claims on appeal and reads as follows:

31. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:
(a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2.;
(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;

(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The prior art references relied upon by the examiner are:

Aligue et al. (Aligue), "Regulation of *Schizosaccharomyces pombe* Wee1 Tyrosine Kinase," J. Biol. Chem., Vol. 272, pp. 13320-13325 (1997)

Hemerly et al. (Hemerly), "Dominant negative mutants of the Cdc2 kinase uncouple cell division from iterative plant development," The EMBO Journal, Vol. 14, pp. 3925-3936 (1995)

Grounds of Rejection

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

These rejections are reversed.

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Background

The subject matter of the present application is generally directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. Specification, page 4. In particular, the claimed invention is directed to a wee1 homologue from maize, zmwee1, whose activity resembles related protein tyrosine kinases. Specification, page 6. The zmwee1 protein is indicated in the specification to be useful in the genetic engineering of the corn plant to increase maize productivity. Specification, page 3.

More specifically, claim 31 is directed to an isolated wee1 nucleic acid comprising a member selected from the group consisting of: a polynucleotide that encodes a polypeptide of SEQ ID NO:2.; a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1; a polynucleotide comprising the

coding sequence set forth in SEQ ID NO:1; and a polynucleotide complementary to a polynucleotide described above.

According to the prior art, Aligue, Wee1 tyrosine kinase regulates mitosis by carrying out the inhibitory tyrosine 15 phosphorylation of Cdc2 M-phase inducing kinase. Abstract. The specification confirms this, stating "induced wee1 overexpression results in phosphorylation of p34 at tyrosine-15 (inactivating p34), effectively blocking the transition from G2 into mitosis." Specification, page 37. The "encoded [wee1] protein is an important part of the checkpoint control machinery that regulates $p34^{cdc2}$ activity and it's [sic] participation in the active MPF (maturation promoting factor) complex." Specification, page 36. Wee1 activity can be stimulated by the CDK2-cyclin A complex, or inhibited by nim1. Specification, page 36.

Description

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

The Federal Circuit has discussed the application of the written description requirement of the first paragraph of § 112 to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of **sufficiently detailed, relevant identifying characteristics** . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613 .

The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to proteins as well as DNAs.

Finally, it is well-settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., In re Herschler, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA 1979): "The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including

those limitations." (citations omitted). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

We apply the relevant law above to the facts before us. In the present case, the examiner argues that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids and transgenic cells, plants and seeds." Answer, page 4. The examiner argues that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 or a polynucleotide complementary thereto, or cells, plants and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." Id.

We find the examiner's argument that one skilled in the art could not predict the structure and function of isolated nucleic acids comprising a wee1 to be confusing in the context of a written description rejection, as predictability is not the legal standard or test for such rejections. However, as best we can understand the examiner's argument, the examiner appears to argue that the specification does not describe a wee1

polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

The examiner argues that "Applicant's [sic] own specification fails to teach a single representative species with 80% identity and WEE1 function." Answer, page 5.

We do not agree with the examiner that claim 31 lacks written description in the specification and that appellants were not in possession of the claimed invention at the time the application was filed. First, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. Thus, we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.

The Enzo court stated that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (*supra*).

In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

The examiner relies on Aligue for the teaching that amino acids 363-408 of the 550 amino acid N-terminal regulatory domain of *S. pombe* WEE1 are critical to the function of the regulatory domain. The examiner concludes that because "the functional properties of WEE1 and other proteins reside in specific amino acid residues, changes in these residues could have an effect on WEE1 function." Answer, page 5.

We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. Those of skill in the art were also aware that the carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented the isolated wee1 having the specific nucleotide and amino acid sequences and variations of these sequences with mutations in described specific areas of Wee1, while avoiding the introduction of mutations in other regions. This teaching, coupled with the ability to test for functional mutants with the assays provided for in the specification, supports appellants' position that the inventors sufficiently described and were in possession of the invention as claimed, at the time of filing of the patent application.

In our view the examiner has not provided sufficient evidence or analysis to indicate why one of ordinary skill in the art having read the disclosure, would not have been able to recognize that the inventors invented the subject matter within the scope of the claims. The rejection of the claims for lack of written description is reversed.

Enablement

Claims 2-11, 31, 33 and 35-36 stand rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

It is the examiner's position that the specification is enabling for an isolated wee1 nucleic acid comprising a polynucleotide encoding SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, but does not reasonably provide enablement for a wee1 polynucleotide having 80% identity to the coding region of SEQ ID NO:1. Answer, page 6.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983), and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Nothing more than objective enablement is required, and therefore it is irrelevant

whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F.2d 162, 192 USPQ 29 (CCPA 1976).

The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. "Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." (footnote

omitted). In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988).

In the present case the examiner provided an analysis of several of the relevant enablement factors on pages 5-9 of the Answer. One of the examiner's primary arguments is that the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. Answer, page 7. The examiner also argues that the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in an alteration of the plant's phenotype." Id.

The examiner relies on Hemerly to support the position that the transformation of plant material is unpredictable in view of the disclosure. According to the examiner, Hemerly teaches "the transformation of *Arabidopsis* and tobacco plants with isolated nucleic acids encoding wild-type and mutant Cdc2a cell cycle regulatory proteins". Answer, page 8. Transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant designed to accelerate the cell cycle unexpectedly did not affect the development of transgenic plants. The transformation of *Arabidopsis* and tobacco with a Cdc2a mutant designed to arrest the cell cycle did affect the development of transgenic plants as expected. Id.

The examiner concludes (Id., pages 8-9)

> Given the unpredictability of determining the function of isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid of SEQ ID NO:1 or isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the absence of guidance in the specification for making and using said nucleic acids and transgenic host cells, plants, and seeds, the lack of working examples, and given the breadth of the claims which encompass multiple polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Analysis of the enablement requirement in the present case dovetails with our analysis with respect to the written description requirement. In particular, the specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Brief, page 9. In addition, the specification page 3, lines 17-31, "describes the level of skill in the art as well as indicating areas of the wee1 gene that can be altered without disturbing substrate recognition." Brief, page 7. Moreover, the specification, page 3, states, "Most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. The carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis."

We agree with appellants that the examiner has not established that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to enable a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

Nor has the examiner established that one of ordinary skill in the art having the chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1 and the ability to test for expression as described in the specification, would be insufficient to transform cells, plants and seeds in view of the success described in the specification. While the examiner relies on Hemerly for the transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant, the examiner has not explained how or why potential unpredictability associated with Cdc2a expression is related to or affects Wee1 expression. Nor is it clear from the examiner's analysis that the examiner has fully considered the state of the art as it relates to the transformation of vectors, seeds and plant cells, as outlined in the specification.

The Patent and Trademark Office Board of Appeals stated:

> The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

In our view, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. The specification, pages 27-29 outlines methods for transfection and transformation of cells and the introduction of DNA into plants. The examples of the specification indicate successful expression of zmwee1 in E. coli as evidenced by the successful inhibition of cyclin-dependent protein kinase. Specification, pages 33-34. In view of the successful transformation of cells with the disclosed and claimed specific wee1, we find no evidence or sufficient indicated reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in transforming cells and plant cells with a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 without undue experimentation.

The rejection of the claims for lack of enablement is reversed.

CONCLUSION

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention is reversed.

The rejection of claims 2-11, 31, 33 and 35-36 under 35 U.S.C. § 112, first paragraph for lack of enablement is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

WILLIAM F. SMITH Administrative Patent Judge	)	
DEMETRA J. MILLS Administrative Patent Judge	)	APPEALS AND
ERIC GRIMES Administrative Patent Judge	)	INTERFERENCES

Appeal No. 2003-1993
Application No. 09/470,526

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Paper No. 36

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte OLGA BANDMAN, JENNIFER L. HILLMAN, PREETI LAL, KARL J. GUEGLER, GINA GORGONE, NEIL C. CORLEY, CHANDRA PATTERSON, and MARIAH R. BAUGHN

Appeal No. 2003-1805
Application No. 09/079,892

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and GRIMES, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 25 through 28 and 33 through 37. Claims 6 through 12 are pending and have been allowed. Claims 29 through 32 are also pending but have been withdrawn from consideration by the examiner. Claims 25 and 33 are representative of the subject matter on appeal. Since claim 25 refers to allowed claim 7, we reproduce claims 7, 25, and 33 as follows:

7. An isolated and purified polynucleotide comprising a polynucleotide sequence as shown in SEQ ID NO:4, wherein said polynucleotide of SEQ ID NO:4 encodes a polypeptide having glutamine fructose-6-phosphate amidotransferase activity.

25. A method for detecting a target polynucleotide in a sample, wherein said target polynucleotide comprises the polynucleotide of claim 7, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

33. An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO:4,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:4,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

The examiner relies upon the following references:

Nishi et al. (Nishi '713)	5,876,713	Mar. 2, 1999
Eur. Pat. App. (Nishi EPA)	EP 824,149 A2	Feb. 18, 1998

Claims 33 through 37 stand rejected under 35 U.S.C. § 112, first paragraph (written description). Claims 25 through 28 and 37 stand rejected under 35 U.S.C. § 103(a). As evidence of obviousness, the examiner relies upon Nishi '713 and Nishi EPA in the alternative. We reverse the written description rejection and affirm the obviousness rejection.

Background

The present invention involves human carbohydrate metabolism enzymes referred to by appellants as "CARM." Specification, page 5. As seen from claims 7, 25, and 33 reproduced above, the claims under review in this appeal involve the polynucleotide sequence as shown in SEQ ID NO:4 which is said to code for CARM-1. Id., page 19, lines 14 through 20. As explained:

> CARM-1 has chemical and structural similarity with human glutamine: fructose-6-phosphate amidotransferase (GI 183082). In particular, CARM-1 and human glutamine: fructose-6-phosphate amidotransferase share 78% identity. A fragment of SEQ ID NO:4 from about nucleotide 243 to about nucleotide 260 is useful, for example, as a hybridization probe. Northern analysis shows the expression of this sequence in various libraries, at least 51% of which are immortalized or cancerous and at least 46% of which involve immune response. Of particular note is the expression of CARM-1 in gastrointestinal, male and female reproductive, and nervous tissues.

Id., page 20, lines 4 through 11.

Discussion

1. Written description.

The examiner considers that claims 33 through 37 do not comply with the written description requirement of 35 U.S.C. § 112, first paragraph, since:

> The specification defines an 'allelic sequence' (see page 10) as an alternative form of the gene which may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered and that any given natural or recombinant gene may have none, one or many, allelic forms, and that common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, substitutions of nucleotides each of which may occur alone or in combination with the others one or more times in a given sequence. This definition does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO:4 (i.e. where are the regions within which mutations are likely to occur) nor discloses any function for naturally occurring variants. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:4 relates to the structure of any naturally

> occurring alleles. The general knowledge in the art concerning alleles does not provide any indication of how one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art structure of one does not provide guidance to the structure of others. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e. the sequence encoding SEQ ID NO:2) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Examiner's Answer, paragraph bridging pages 3 and 4.

The examiner also

> [F]ully acknowledges appellants' recitation of the structural limitations of the polynucleotides of claim 33 parts b) and d)-e). However, the polynucleotides as defined in claim 33 parts b) and d)-e) encompass a genus of polynucleotides that encompasses widely variant species, some having the same functions as the polypeptide of SEQ ID NO:1, some having unknown and distinctly different functions and some possibly having no function. While one of skill in the art, provided the polynucleotide sequence of SEQ ID NO:4, may be able to recognize variants of SEQ ID NO:4 with nucleotide sequence sharing 90% identity, one cannot recognize which of these variants occurs naturally and is thus encompassed by the genus of claim 33 part b). Therefore, the skilled artisan would not be able to recognize a member of the claimed genus of polynucleotides merely from its structural definition. This enormous genus will encompass a wide variety of polynucleotides with their own distinct properties. Because appellants have provided no functional limitation for the claimed polynucleotides, the single disclosed polynucleotide of SEQ NO:4 is not representative of the entire genus and one of skill in the art would not recognize that appellants were in possession of all polynucleotides comprising a naturally-occurring polynucleotide having at least 90% identity to SEQ ID NO:4 as encompassed by the claims.

Examiner's Answer, paragraph bridging pages 11 and 12.

The Federal Circuit discussed the application of the written description requirement to inventions in the field of biotechnology in University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), stating

that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials" Id. at 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. at 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

In reviewing this rejection, we note that the examiner has not rejected claim 8 under this section of the statute. Claim 8 reads:

8. An isolated and purified polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to the polynucleotide of SEQ ID NO:4, wherein said naturally occurring polynucleotide sequence encodes a polypeptide having glutamine-fructose-6-phosphate amidotransferase activity.

As seen, claim 8 differs from claim 33 b) which is the focus of the examiner's written description rejection in that it adds the limitation that the naturally occurring polynucleotide sequence encodes a polypeptide having glutamine-fructose-6-phosphate amidotransferase activity. Since the examiner has conceded that a claim having the scope of claim 8 complies with the written description requirement of 35 U.S.C. § 112, we do not find that the lack of a statement of function in claim 33 b) means that that portion of the claim lacks written descriptive support.

Claim 33 b) defines a genus of polynucleotides by way of two significant qualifiers. First, the polynucleotide of claim 33 b) must be "naturally occurring." Second, the polynucleotide of claim 33 b) must be "at least 90% identical to the polynucleotide sequence of SEQ ID NO:4." As explained in Lilly, a genus of polynucleotides can be described by a representative number of polynucleotides sharing common structural features which constitute a substantial portion of the genus. The examiner is correct in his analysis that claim 33 b) includes so-called nonfunctional alleles. However, those nonfunctional alleles must be "naturally occurring" and be at least "90% identical to the polynucleotide sequence of SEQ ID NO:4." In our view, these two limitations adequately describe the genus of polynucleotides encompassed by claim 33 b) without that claim further including a functional limitation.

We understand the examiner's concern that one may not recognize that a polynucleotide sequence having 90% identity with that of SEQ ID NO: 4 is "naturally occurring." However, that concern is more properly raised under a rejection under 35 U.S.C. § 112, second paragraph, rather than the written description requirement of the first paragraph.

The written description rejection is reversed.

2. Obviousness.

We initially note that appellants state that the claims are grouped together for the purposes of this rejection. Appeal Brief, page 5. Accordingly, we shall decide the issues raised in the Examiner's obviousness rejection as they pertain to claim 25. 37 CFR § 1.192(c)(7). We also note that the two Nishi references relied upon by the examiner appear to be the same. Thus, we shall consider the merits of the examiner's rejection as it is based upon Nishi '713.

Claim 25 is directed to a method for detecting a target polynucleotide said to comprise the polynucleotide of claim 7 in a sample. To this end, a sample is hybridized with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample. The probe will specifically hybridize to the target polynucleotide, if present, forming a hybridization complex. The presence or absence of the hybridization complex is an indication as to whether the sample contained the target polynucleotide.

The examiner has determined without dispute by appellants that Nishi '713 describes a polynucleotide encoding a carbohydrate metabolizing enzyme (glutamine:fructose-6-phosphate amidotransferase activity) that is 100% identical to the amino acid sequence set forth in SEQ ID NO:1 of this application. Examiner's Answer, page 6. The examiner has also determined, again without dispute by appellants, that Nishi '713 describes a polynucleotide sequence encoding that polypeptide that is 67.7% identical to the polynucleotide sequence set forth in SEQ ID NO:4 of this application. Id. The basis for the examiner's findings are the sequence comparison printouts

obtained as a result of an electronic search of sequence databases. As seen from the sequence search report dated December 14, 1999, U.S.-09-079-892-4.rng, pages 1-3 the polynucleotide sequence extending from nucleotide 99-2144 of SEQ ID NO:4 of this application is 100% identical to the coding sequence set forth in Nishi '713. See, e.g., Figs. 2A-2F and SEQ ID NO:5 of Nishi '713.

The examiner has concluded that it would have been obvious to a person of ordinary skill in the art to use any 20 contiguous nucleotides in the region of the polynucleotide sequence described in Nishi '713 as a probe in either a hybridization reaction or as part of a set of probes/primers in a PCR reaction to detect a target polynucleotide. Once again, appellants do not dispute this aspect of the examiner's position. Indeed, Nishi suggests as much, stating:

> The DNA encoding the protein or the partial peptide of the present invention can be cloned either by PCR amplification by using synthetic DNA primers having a partial nucleotide sequence of the DNA coding for the protein or by hybridization using the DNA inserted in a suitable vector and labeled DNA fragment or synthetic DNA coding for a part or full region of the protein or the partial peptide of the present invention. The hybridization can be carried out by the method described in Molecular Cloning, 2nd (J. Sambrook et al., Cold Spring Harbor Lab. Press, 1989). When a commercially available DNA library is used, the instructions given in the accompanying manual can be followed.

Nishi '713, column 15, lines 54 through 65.

Where the appellants and the examiner part company in regard to the obviousness rejection has to do with whether claim 25 on appeal is "directed only to detecting the target polynucleotides, comprising the polynucleotides recited in claim [] 7 . . ." (Appeal Brief, page 12) or whether claim 25 is inclusive of "detecting any target polynucleotide which hybridizes to probes generated from the sequence of

Nishi. . .." (Appeal Brief, page 11) (emphasis in each original). Appellants urge that claim 25 must be read such that the claimed method detects only the polynucleotides recited in claim 7. We disagree with appellants' claim construction.

First, appellants' position does not take into account that claim 25 explicitly reads upon a negative result, i.e., the probe comprising at least 20 contiguous nucleotides will not hybridize to any nucleotide sequence in the sample. This is seen in that claim 25 b) includes detecting the absence of a hybridization complex. Since appellants have not contravened the basic premise of the examiner's obviousness rejection, i.e., it would have been obvious to one of ordinary skill in the art to use a probe comprising at least 20 contiguous nucleotides based upon the polynucleotide sequence described in Nishi '713 in a hybridization method, the performance of such a method that results in a negative result reads directly upon claim 25. Thus, the examiner's rejection can be sustained on this basis.

Second, we do not read claim 25 in the manner in which appellants do. In our view, claim 25 is not limited "only to detecting the target polynucleotides comprising the polynucleotides recited in claim [] 7 . . .." Appeal Brief, page 12. Once a probe comprising at least 20 contiguous nucleotides is constructed based upon the polynucleotide sequence described in Nishi '713, the use of that probe in a hybridization method will result in the hybridization complex being formed if the probe hybridizes to any polynucleotide sequence in the sample under the hybridization conditions used. Thus, an appropriately constructed probe based upon the polynucleotide sequence described in Nishi '713 will hybridize to a polynucleotide sequence such as that of Nishi

'713, that of SEQ ID NO:4 of this application or any other polynucleotide sequence having sufficient complementarity given the hybridization conditions used.

The examiner's obviousness rejection is affirmed.

The decision of the examiner is affirmed-in-part.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

Sherman D. Winters Administrative Patent Judge	)
William F. Smith Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Eric Grimes Administrative Patent Judge	)

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